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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/918,601	07/30/2001	Garry P. Nolan	A-64260-5/DJB/RMS/AMS	6631

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EXAMINER
WESSENDORF, TERESA D

ART UNIT	PAPER NUMBER
1627	

DATE MAILED: 08/14/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/918,601	Applicant(s) NOLAN, GARRY P.	
	Examiner T. D. Wessendorf	Art Unit 1627	

-- The MAILING DATE of this communicati n appears on the cover sheet with the correspondence address --

Peri d f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *23-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6,7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *cRF Report* .

DETAILED ACTION

The CRF submitted on 11/06/01 does not comply with the sequence requirement of 37 CFR 1.821-1.825 because the CRF was unreadable. See attachments.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 47-58 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter and lacks patentable utility.

The claimed molecular library of retroviruses comprising at least 10 different biased randomized nucleic acids or a cellular library of mammalian cells is a non-statutory subject matter since these libraries will read on naturally occurring retroviruses or mammalian cells that contain a library of different components which undergo mutations similar to the instant claimed biased random library. Furthermore, these libraries are merely starting materials, like those found in nature, and are nothing more than a conglomerate or combinations

of all kinds of components, from which a particular product(s) is being isolated, purified and identified. However, 35 USC 101 is clear in its requirement that a patent is granted for a **useful product** and not a starting material from which a product can be obtained.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 47-58 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 23-58 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific library as provided in Figs. 1 and 2 (Example 2), a tumor cell and other specific embodiments disclosed in the specification does not reasonably provide enablement for the broadly claimed variables encompassed by the claimed method and library. The specification does not enable any person skilled

in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The claimed invention recites infinite and undefined variables such as cells and the different phenotypes exhibited or undergone by said cells; the library of biased and random peptide wherein the location of the biased or random sequence is unknown, the kind, length of amino acid residues comprised in each of the biased or random sequences especially since the biased library exerts different effects like the minimization of stop codon or reaction with different class molecules, the size and/or the complexity of the library; the candidate nucleic acid that transcribed and translate into an agent; the kind of agent; the class of molecules and other broad classes of compounds or variables that are too numerous to mention specifically. The specification discloses, as stated above, only specific parameters that results in a specific bioactive agent. Other than the specific guidance and/or direction, the disclosure contains nothing more than generalized statements. There is nothing in the disclosure that indicates that the specific embodiments provided therein can be extrapolated or predicted from these specific embodiments. Lacking such disclosure the broad claimed invention encompassing

every conceivable variable entails undue amount of experimentation.

The factors that are to be considered in the determination of undue experimentation includes: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the art, the predictability of the art and the breadth of the claims.

1). The specification fails to give adequate direction and guidance in how to readily go about determining a bioactive agent present in a biased and random library of undefined and/or infinite composition, i.e., the different nucleic acids (n.a.) that would encode a peptide, especially in view of the known degeneracy of the n.a. codons; the size of the library comprising the different peptides, the method steps expressing the candidate peptides in a plurality of cells and the screening steps that would give the lead peptide; the type of cell population that can be altered and the phenotype altered and the different conditions necessary to screen, isolate the cell and identify the agent. Furthermore, the specification does not provide adequate direction with regards to the type or size of library of nucleic acid encoding said peptide or the expression

package of the nucleic acid; where one can make insertions in an expression system so as not to cause deleterious effects on the viral vector, there is no direction and guidance concerning how to determine which sites will not affect the viral life cycle such as the ability of the virus to attach and enter a cell. The nucleic acid fusion libraries may contain so many inserts per viral vector that the synthesis of the inserts produces an observable effect on the host metabolisms. Because of this, there is very significant censorship of the library due to a broad set of selection factors ranging from proteins synthesis to virion assembly.

2). Applicants have failed to provide any working example for any library of nucleic acid in any retroviral vector transfected into any organisms such as virus, yeast or bacteria, except, of course, for the retroviral as shown in Fig. 1 using specific method steps.

3). The state of the prior art is such that the consequences of some agent and cell interaction and/or effect of said bioactive agent on some cells have not yet been fully or clearly elucidated.

4). The art is inherently unpredictable with respect to the numerous types of nucleic acid that encodes a peptide especially in view of the degeneracy of the codons, the

bioactive agent itself that confers an unknown effect to a given cell population, the vectors use in nucleic acid expression or display wherein even if one surface protein is identified as a candidate peptide it is not possible to predict what effect the insertion of other peptide into the viral protein will have on the peptide or the vector package *a priori*. Also, the use of a wide variety of libraries with peptide presentations can be displayed in an extraordinarily large number of conformations.

5). The breadth of the claims encompasses a large possible combinations for the different recited variables such as the large diversity of library of nucleic acid that encodes a bioactive agent peptide, the bioactive agent effect in the cell population and/or isolation and identification and cell population itself and other infinite variables as recited above.

6). While the level of skill in the art is perhaps, high, the molecular biology and gene art is so unpredictable that it would require undue experimentation to make the invention commensurate in scope with that claimed in the absence of adequate guidance or direction as set forth above. [It is suggested that applicant recites in the claims the method steps as disclosed in Figs. 1 and 2 with the specific biased random

library of nucleic acid, tumor cells and other embodied species as recited in the Examples.]

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 23-58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A). Claims 23-58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language. This claim is an omnibus type claim.

Claims 23 and 24 are unclear as to whether an altered cell phenotype or a bioactive agent is the one being screened or both. It is not clear, within the claimed context, the basis of a candidate nucleic acid. The term "minimize" is a relative term, the measure or basis by which said stop codon is minimized is not clearly set forth in the claims. The metes and bounds of the claimed "phenotype", "cell", "transdominant intracellular bioactive agent", "molecular library of biased randomized nucleic acids", "class of molecules" are not clearly set forth.

Claim 24 is confusing as to whether the phenotype alteration is due to the interaction of the biased residues to a class of molecules.

B). Claims 25 and 26 do not further limit the steps of the base claims. Obviously the steps in the base claim contain the essential steps recited in claims 25 and 26 before identification can be done. [It is suggested that applicants incorporate the step in the base claims.]

C). Claim 27 broadens claim 26. The step in claim 27 is an additional step that does not further limit claim 26. Claim 26 or the base claim does not recite for isolating a "target molecule" only identifying an agent that alters a cell phenotype. It appears that a different compound, the target molecule is additionally being claimed.

D). Claim 29 is confusing as to the molecules included in the SH3 or SH2 domains or death domains and to the other recited compounds. The grouping of these compounds in Markush is an improper one. There is no common feature for each of the different compounds and includes both a genus and species groups as the enzymes. Within the claimed context, what would constitute a class of compounds as the death domains or the domain it encompasses?

E). Claim 30 broadens the base claim, which does not recite a presentation sequence. Within the claimed context, what are the metes and bounds of the claimed "presentation sequence" and "conformationally restricted **form**"? The term "capable" connotes uncertainty as to whether, in fact, said presentation of the product occurs in a conformationally restricted form.

F). Claims 33-37 are unclear as to whether the exponential numbers refers to the different amino acid in the biased or random or both library or thee size of the library. Cf. with page 20, lines, and 20-25 of the instant specification. "At least" does not recite the maximum limit, especially in the absence of positive recitation in the specification.

G). Claims 38-46 broadens the base claim. The base claim does not recite a conjugate for the n.a. or the encoded bioactive agent. The metes and bounds of these sequences are indefinite since these sequences as recited in claims 40-46 are different in structure, kind and/or length or other characterizing features.

H). The recited "at least 10" different biased randomized n.a. is unclear as to whether said number refers to each of the biased or randomized n.a. or to both libraries. The metes and bounds of said 'at least' is not positively recited in the specification.

I). Claims 53-56 broadens the base claim. The base claim does not recite for a fusion partner. The metes and bounds of these sequences are indefinite as they contain different kind, length, sequences and whether the whole or part of each of said sequences are claimed.

J). Claim 58 recites limitation already present in the base claim and merely constitutes a re-wording of the base claim.

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefore ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 23-46 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-27 of prior U.S. Patent No. 6,153,380 ('380 Patent). This is a double patenting rejection.

The instant claims are identical to the claims of the '380 Patent, except worded differently. Is this merely a matter of semantics?

Applicant is advised that should claims 23-46 be found allowable, claims 1-27 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 23-46 are rejected under the judicially created doctrine of obviousness-type double patenting as being

unpatentable over claims 1-12 of U.S. Patent No. 6,365,344('344 Patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant broad claimed method encompasses the method of the '344 except the library of the instant method is a biased random library. However, it is considered that the random library of the '344 patent covers the instant library. The method steps in the '334 Patent contains a biased and random library. (See e.g., the Experimental section at col. 6,lines 25-col. 8 of the '344 Patent disclosing said biased library with a random library.) The '344 Patent appears to claim the same method except worded differently. Is this merely a matter of semantics?

Claims 23-58 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 23-38 of copending Application No. 09/727,715('715 application) or 09/916,940 or 08/963,368 or 08/787,738. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claimed method and molecular library are included in the method and molecular library of the **e.g.**, '715 application, except the instant claimed method and library recites for a different component e.g., stop codons of the same library for the instant method and for the '715 application reciting

different part of the n.a. sequence i.e., reporter sequence. This reporter sequence is obviously required for the instant method to enable identification of a bioactive agent, the same bioactive agent being identified in the '715 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (703) 308-3967. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-7924.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

T. D. W

T. D. Wessendorf
Primary Examiner
Art Unit 1627

Tdw

8/12/02